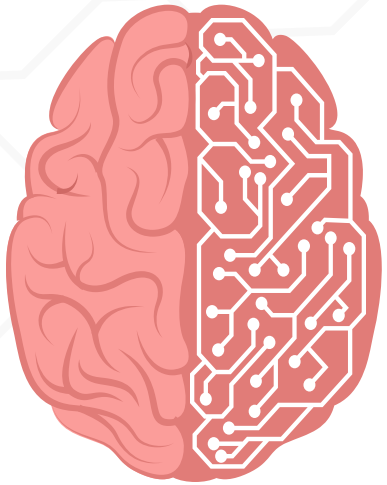

Physiology - GUS

Done By

Heba Al Tahat

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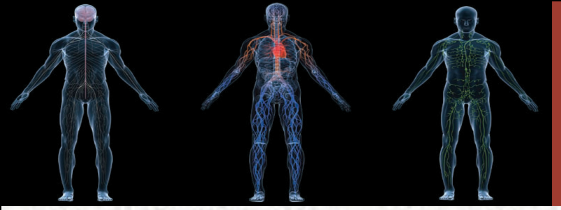
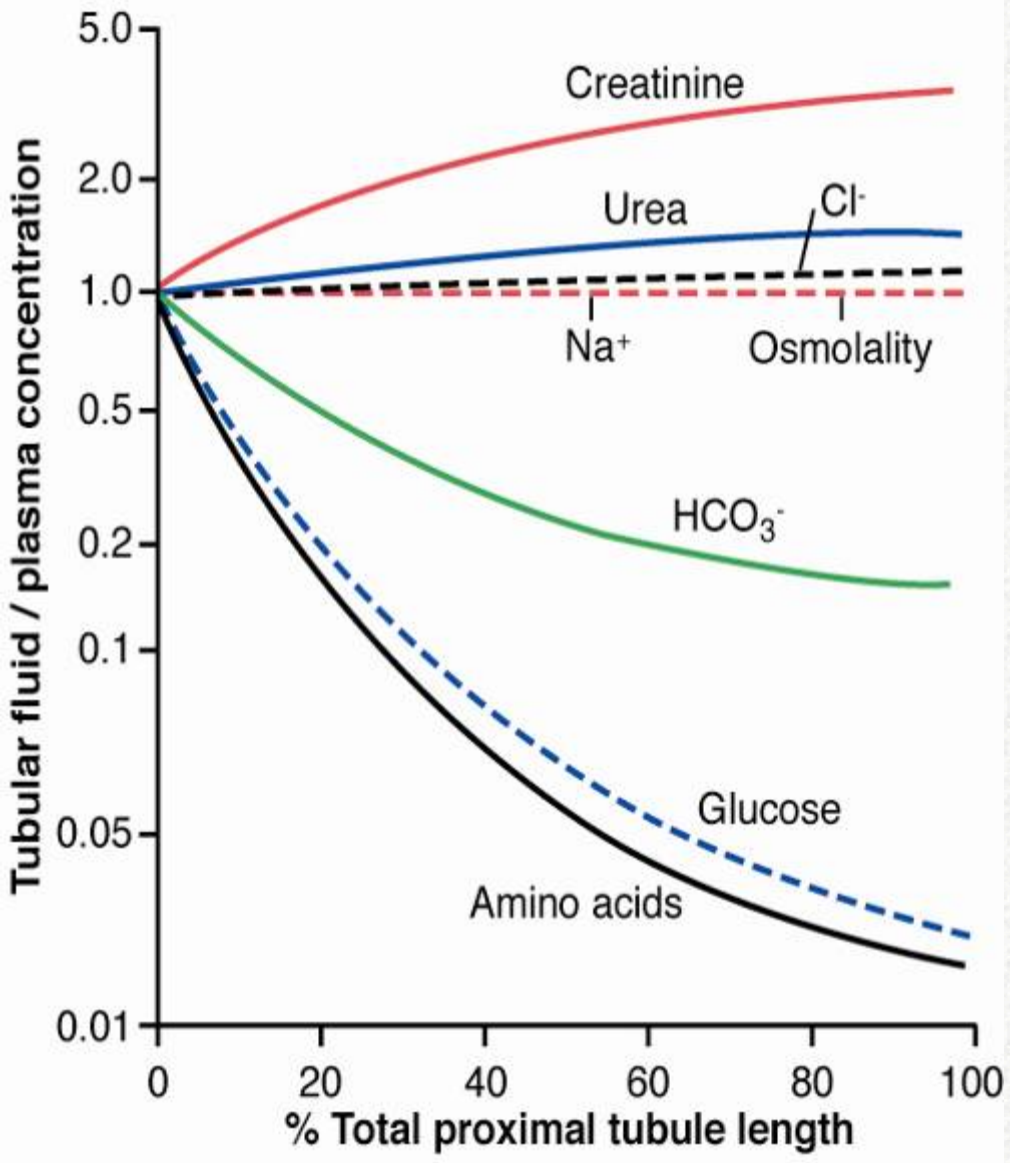


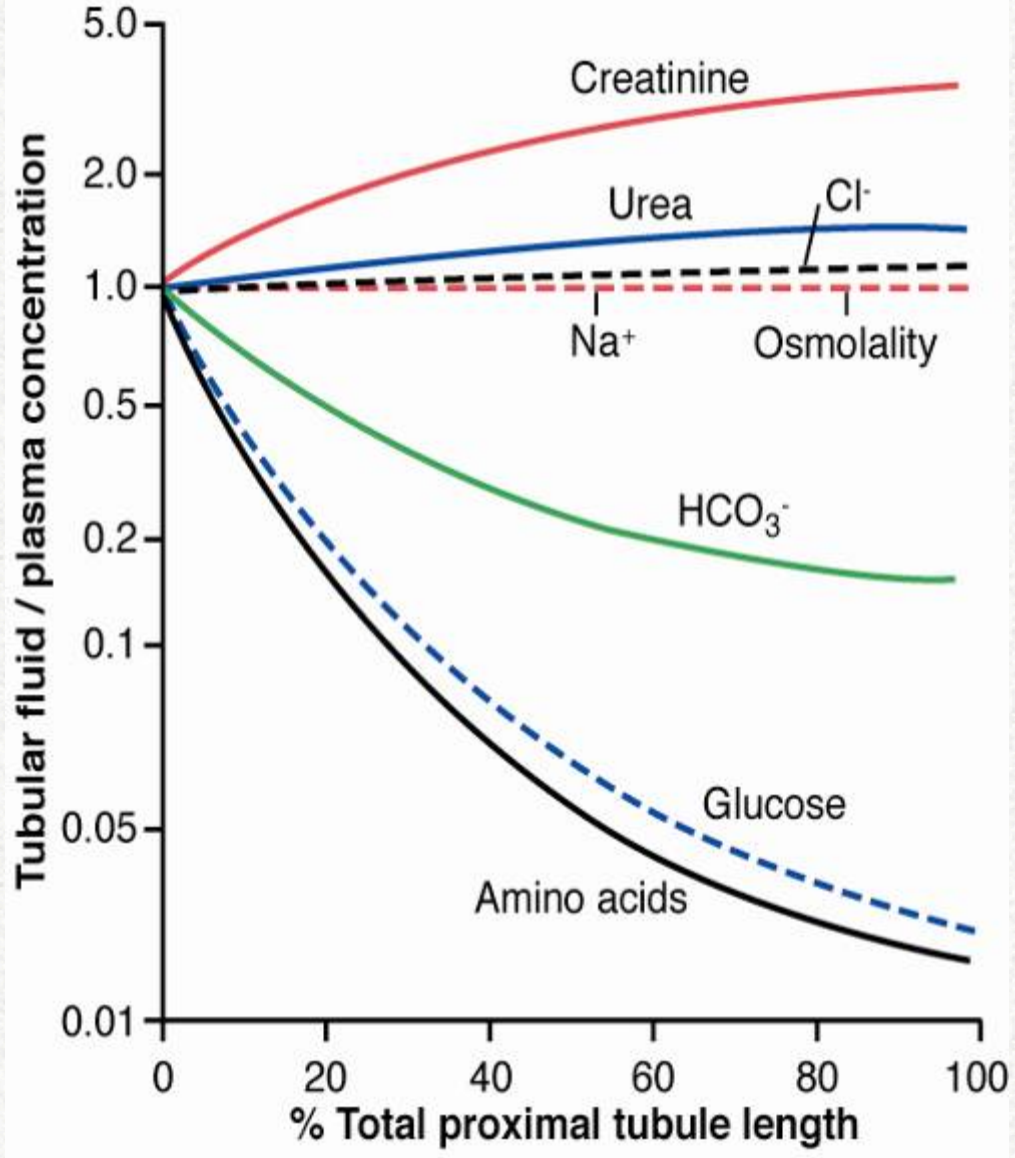
Changes in concentration in proximal tubule



- We can trace different substances in the proximal convoluted tubule by measuring tubular fluid/plasma concentration ratio.
- Along the length of the proximal convoluted tubule, some of the substances have a ratio higher than 1, while others are lower than 1, and some are around one.
- The osmolality of the substance in the tubular fluid depends on the concentration or amount of the substance in the tubular fluid in this part of the nephron (is there extensive reabsorption or poor?) and also the plasma concentration of the substance along the nephron.
  The reabsorption of the substance along the nephron does not affect the plasma concentration of that substance, its concentration stays almost constant, and this is because the amount of the tubular fluid in one nephron is almost negligible compared the amount of the whole plasma and so even if it changes it will not affect the overall concentration of the substance in the plasma.
- This means that when there is a change along the nephron in the concentration of a substance this reflects the tubular concentration rather than the plasma concentration.

Figure 27-7

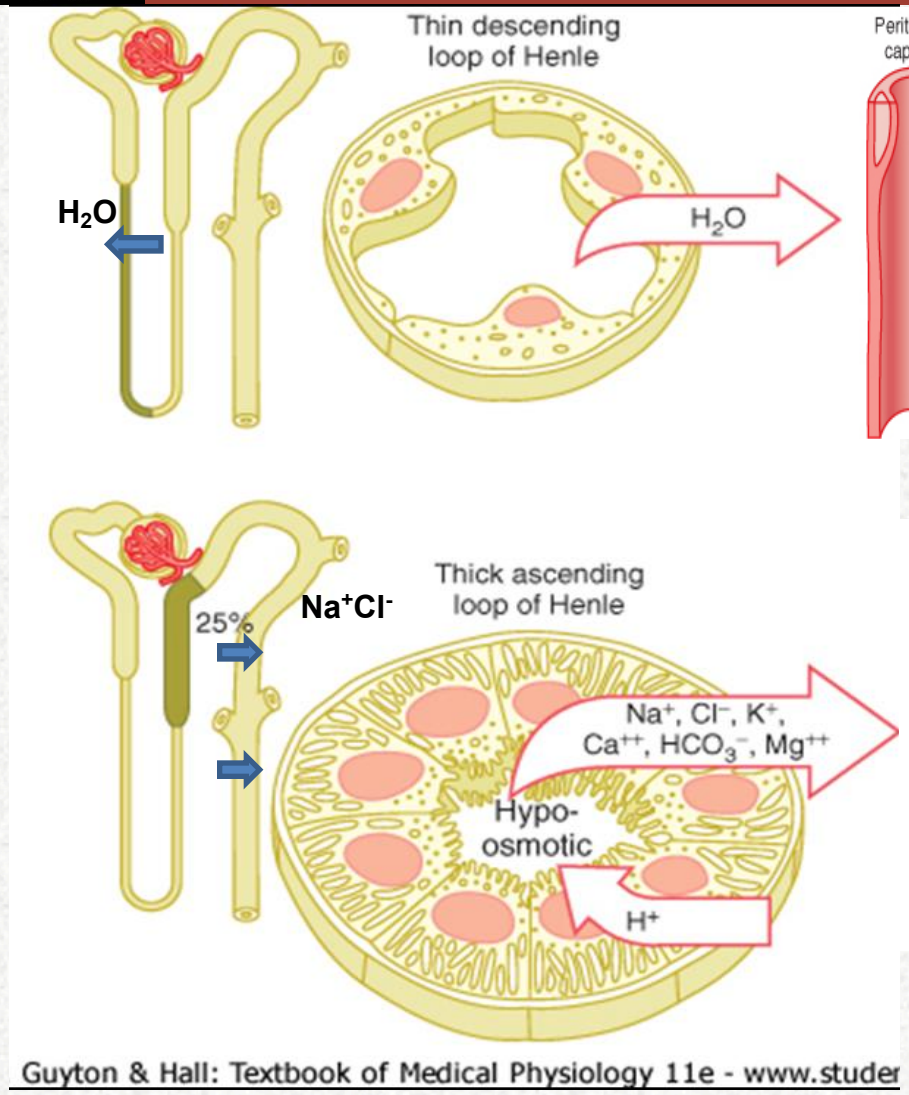
Changes in concentration in proximal tubule



- Another thing that affects it is the ratio of the water reabsorption/the substance reabsorption.
- If water reabsorption is way more than the substance reabsorption, then the ratio will be more than 1, examples are creatinine and urea (because they are waste products).
- If the water reabsorption is less than the substance reabsorption, then the ratio is less than 1, and if there is complete reabsorption then the ratio will reach zero, such as with glucose and amino acids.
- Sodium and chloride are around 1, so they are reabsorbed at almost the same rate as water.
- This ratio can be measured in all segments.

Figure 27-7

Loop of Henle

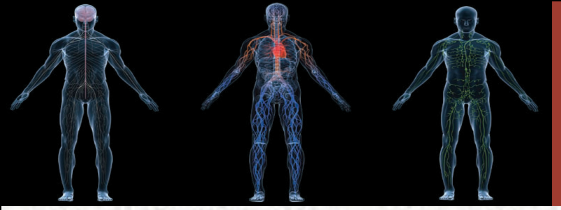


Thin Descending
- ❑15% of filtered H_2O reabsorbed.

Thin Ascending
- ❑Passive reabsorption of Na+, K+, Cl-.
- ❑Impermeable to H_2O.

Thick Ascending
- ❑25% of Na+, K+, Cl-HCO_3^-, Ca^{++}, Mg^{++} reabsorbed.
- ❑Impermeable to H_2O.
- ❑Called = Diluting segment.
- ❑Secretion of H^+

- Functional segments in loop of Henle: thin descending, thin ascending and thick ascending.



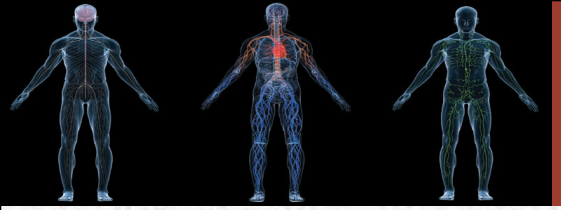
Loop of Henle

- The thin descending segment is highly permeable to water, and it depends on the type of epithelial cells that line the tubules, in this segment the cells allow for the passage of water, the tight junctions allow for water to pass through, and there are aquaporin channels that allow for passage of water through the transcellular route as well.
- Here the solute permeability is less than the permeability for water, so the main affect of these characteristic of this segment of the tubule is passive reabsorption of water (osmosis).

- Both the thin and thick ascending are almost not permeable to water but they are permeable to solutes (Na+, Cl-).

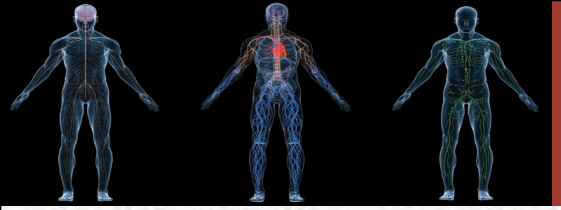
- In the thin ascending segment, the epithelium is not packed, not with organelles for energy production or with transporters, so the main activity is simple or passive transport of solutes until there is equilibrium between the interstitium and the tubular fluid. There is no active process

- In the thick ascending segement, it is also impermeable to water but it is packed with organelles that produce energy and Na+-K+ ATPase channels and pumps and transporters, so there is active transport of solutes in this segment.
- 25% of Na+Cl- is absorbed in the thick ascending limb of Henle and because it is impermeable to water so this segment is responsible for dilution of the tubular fluid and the thick ascending is called diluting segment



Loop of Henle

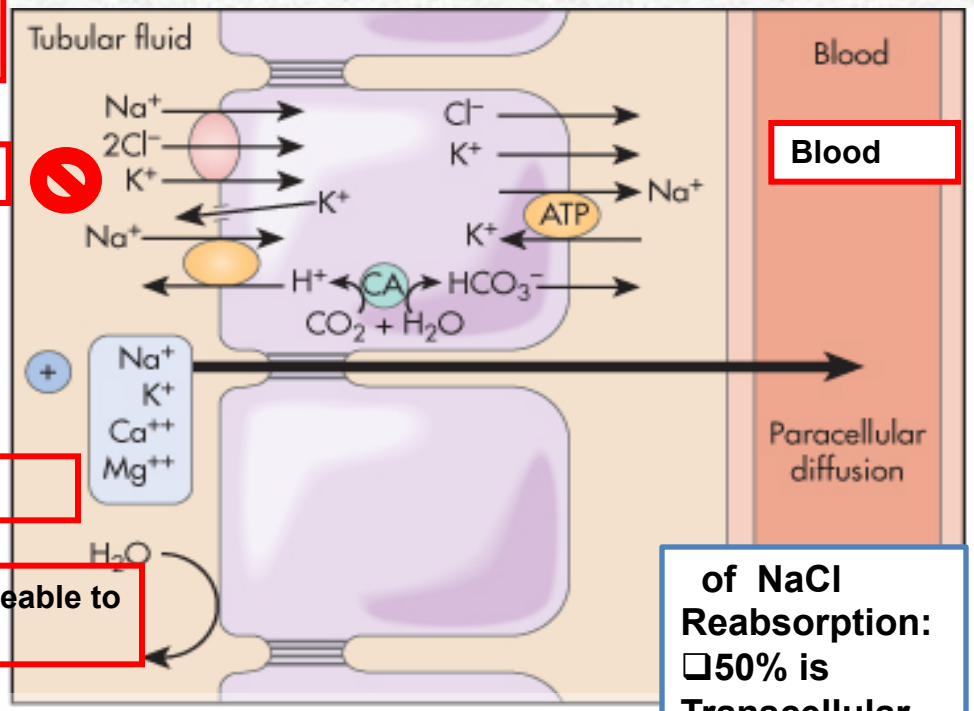
- Water reabsorption occurs exclusively in the **thin descending** limb of Henle via AQP1 water channels.(**Aquaporins**)
- Reabsorption of **NaCl** occurs in both thin and thick **ascending** limb of Henle.
- In thin ascending limb NaCl is reabsorbed passively. However, in thick ascending limb NaCl is reabsorbed through Na^{+}-K^{+} ATPase in basolateral membrane ans .
- Ascending limb is impermeable to water.
- Reabsorption of Ca^{++} and $HCO3^{-}$ occurs also in Loop of Henle.



Thick ascending limb of Henle

Tubular fluid

Furosemide



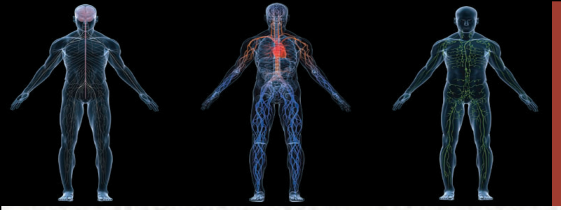
Blood

Voltage

Impermeable to water

of NaCl Reabsorption:
- **50% is Transcellular**
- **50% is Paracellular**

- There is a transporter called the 1Na+,2Cl-1K+ transporter, it is present in the apical (luminal) side of the epithelial cells, it facilitates the reabsorption of these ions and then they get diffused into the interstitium and then to the peritubular capillaries. The driving force for this transport is the gradient caused by the Na+-K+ ATPase channel (which is present on the basolateral side)
- Another important transporter, the Na+-H+ exchanger, causes the absorption of sodium and secretion of hydrogen ions, and this is our way of getting rid of acids in our bodies. The hydrogen ion results from the dissociation of carbonic acid into H+ and HCO3- after the reaction of water and CO2 catalyzed by the enzyme carbonic anhydrase; the hydrogen ion is secreted and the bicarbonate ion is reabsorbed.



- Paracellularly, in the thick ascending tubule, there is a generation of a more positive luminal charge, and this is caused by a potassium leak from inside the cells into the lumen. This positive charge causes the repulsion of the positive ions in the lumen that these ions go to be reabsorbed by the paracellular route separately from water. The driving force is higher the more positive (bivalent) the ion is. This is called the voltage drag.

- There is a drug called furosemide that blocks the 1Na+,2Cl-.1K+ transporter. This drug is used for relieving hypertension quickly. Its MOA is the blockage of this channel which will block the reabsorption of Na+-Cl-, this will increase the concentration of solutes in the overall tubular fluid and water will be absorbed less in other segments of the tubules (this one is impermeable) and the urine volume will increase, while the blood volume decreases (relieves hypertension). This is called diuresis.
- The problem with this drug is that it also prevents the reasbsorption of potassium and so it is lost in the urine, and this causes hypokalemia (very dangerous for the heart activity and function), in long term use.

Sodium chloride and potassium transport in thick ascending loop of Henle

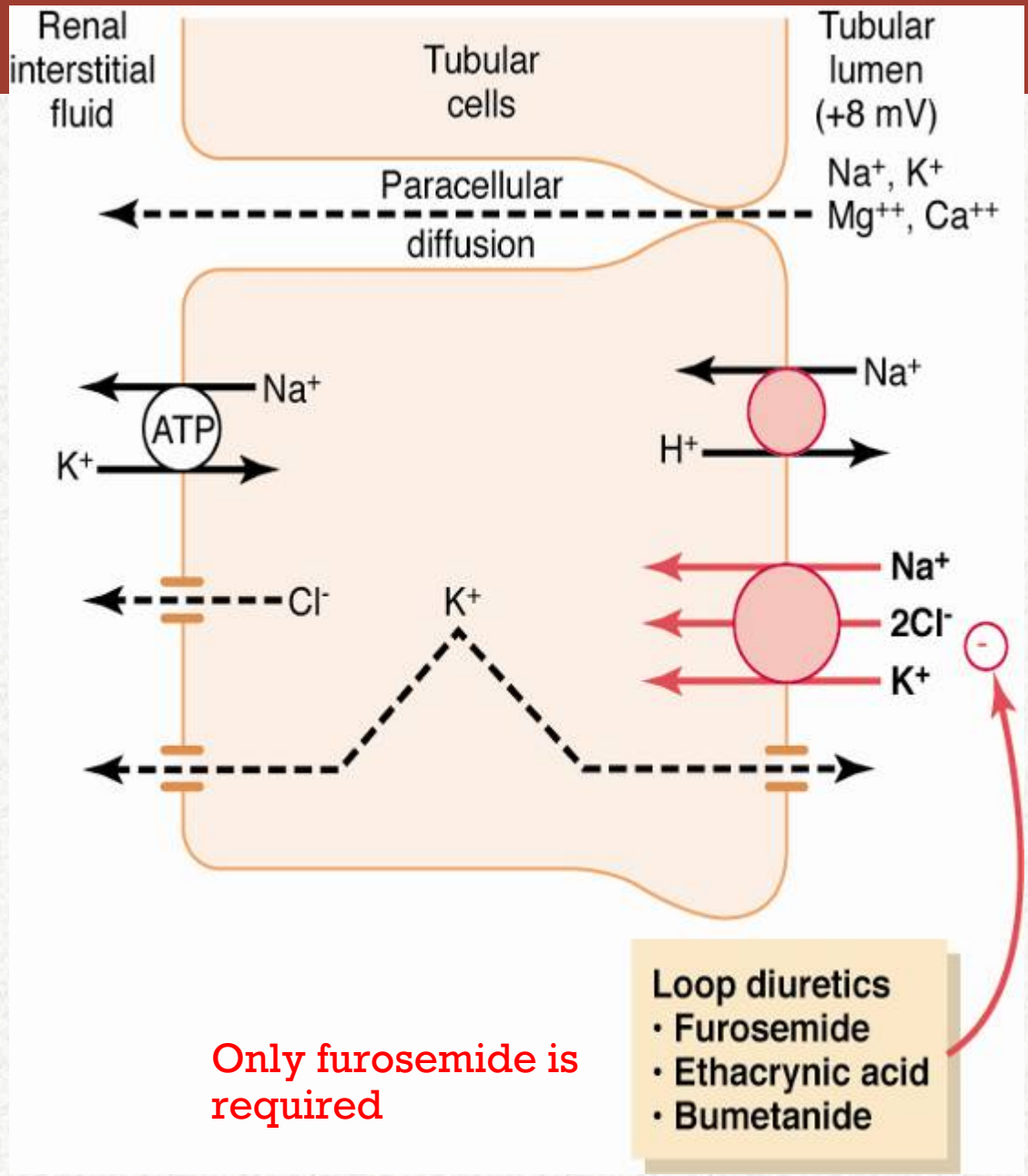


Figure 27-9

Early Distal Tubule

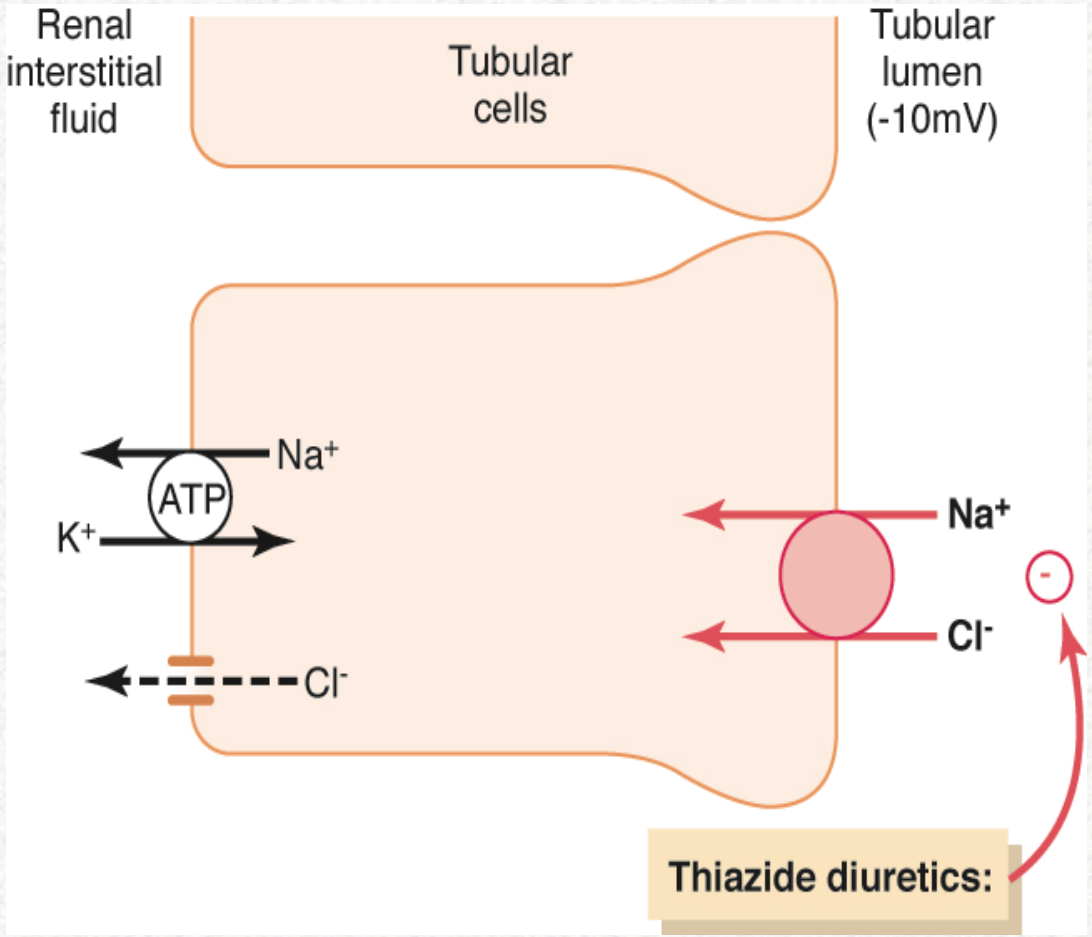
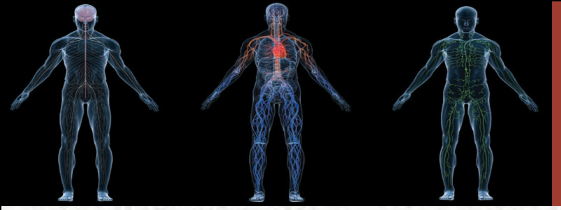


Figure 27-10

- The first cells in the early distal tubule is called macula densa, it plays a role in tubular glomerular feedback, in the juxtaglomerular apparatus.
- Macula densa is usually either a part of the early distal tubule or the end of the thick ascending limb.
- The early and late distal tubules are two functionally different parts, they each have separate characteristics.
- The early distal tubule has a channel on its luminal side called the Na+-Cl- co transporter which cause the reabsorption of sodium and chloride with the help of the Na+-K+ ATPase pump.
- There is a diuretic called thiazide that blocks this channel, when they block it in this segment, and this causes diuresis and it is a treatment for hypertension.



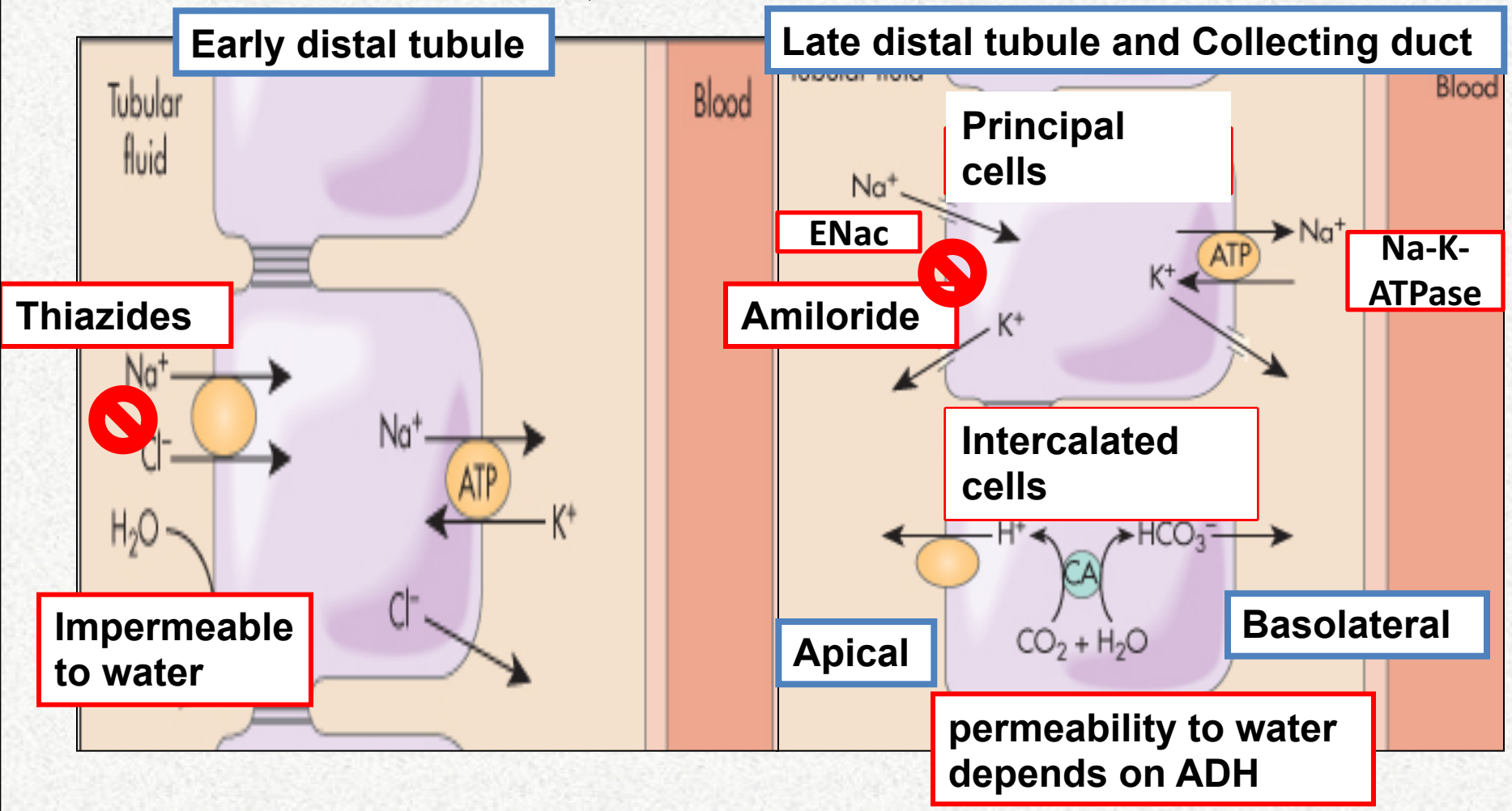
Early Distal Tubule

- Functionally similar to thick ascending loop
- Not permeable to water (called diluting segment)
- Active reabsorption of Na^+, Cl^-, K^+, Mg^{++}
- Contains macula densa

The thick ascending tubule is the main diluting segment, but this part contributes to the dilution.

Distal tubule and collecting duct

- Reabsorbs 7% NaCl, secrets K+ and H+ and reabsorbs 8-17% H_2O



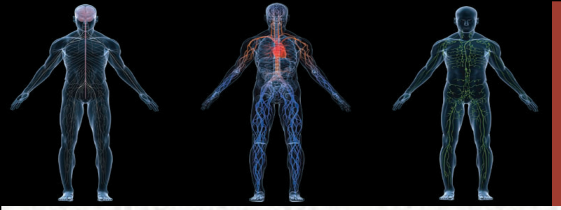
- We are gonna talk about the late distal and collecting duct together because they are functionally similar.
- They are formed of two types of cells, principal cells and intercalated cells.

- Functionally, principal cells are the site of action for aldosterone. There is a channel on their luminal side called the epithelial sodium channel (ENac), and aldosterone increases the activity of this channel, and increases the reabsorption of sodium (driving force from Na+-K+ ATPase once again). Here the reabsorption of sodium is accompanied with the secretion of potassium.
- So, another function for aldosterone, other than increasing blood pressure by sodium reabsorption, is the reduction of the potassium level, hyperkalemia also induces the secretion of aldosterone.

- Amiloride is a drug that was designed to block ENac channels, this will cause diuresis because it prevents the reabsorption of sodium, but here potassium is spared, there will be an increase of K+ in the blood. So, this drug differs from other diuretics in that they cause the loss of potassium, but this one called a potassium sparing diuretic.

Intercalated cells play a very important role in acid-base balance, because they have a transporter called the hydrogen ATPase, it secretes hydrogen ions. It is works 1000x more than the Na+-H+ channel in the thick ascending tubule, and so it is more efficient in secretion of hydrogen, even if it was against the gradient.

- The permeability to water in the late distal tubule and the collecting ducts is variable, they depend in the availability of ADH (anti-diuretic hormone). In the presence of ADH there is insertion of aquaporin channels into the luminal membrane, and they become permeable to water, but if it is absent the aquaporin channels remain sequestered inside the cell, and it is impermeable to water.
- Since the tubular fluid has just gone through the diluting segments then the tubular fluid will have plenty of water and in the presence of ADH water reabsorption will occur, this causes decreased volume of urine and increase in its concentration. So, the function of ADH is the concentration of urine and preserving water in our bodies.



Early and Late Distal Tubules and Collecting Tubules.

These segments (cortical) are not permeable to urea, so there is no reabsorption of urea, but the medullary colleting tubules are characterized by being permeable to urea.

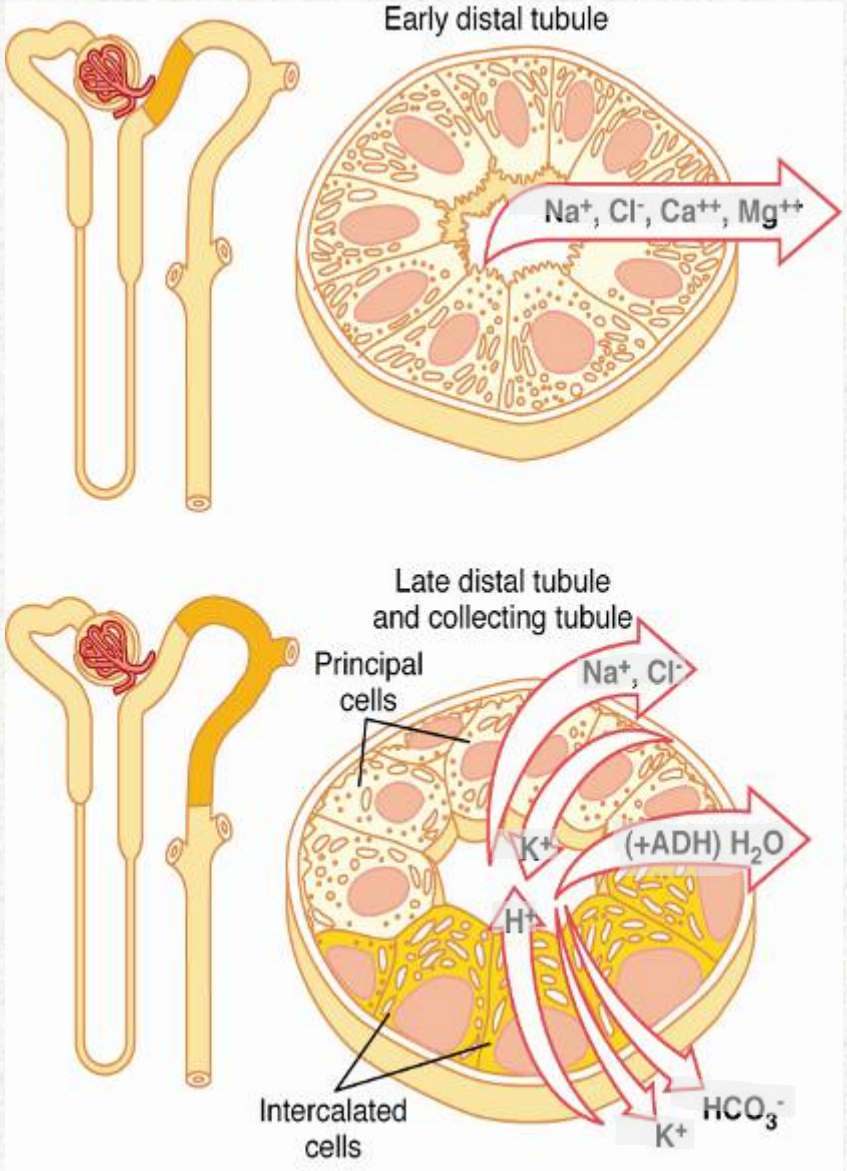


Figure 27-11

~ 5% of filtered load NaCl reabsorbed

- not permeable to H_2O
- not very permeable to urea

- permeablility to H_2O depends on ADH
- not very permeable to urea

Late Distal and Cortical Collecting Tubules Principal Cells – Secrete K^+

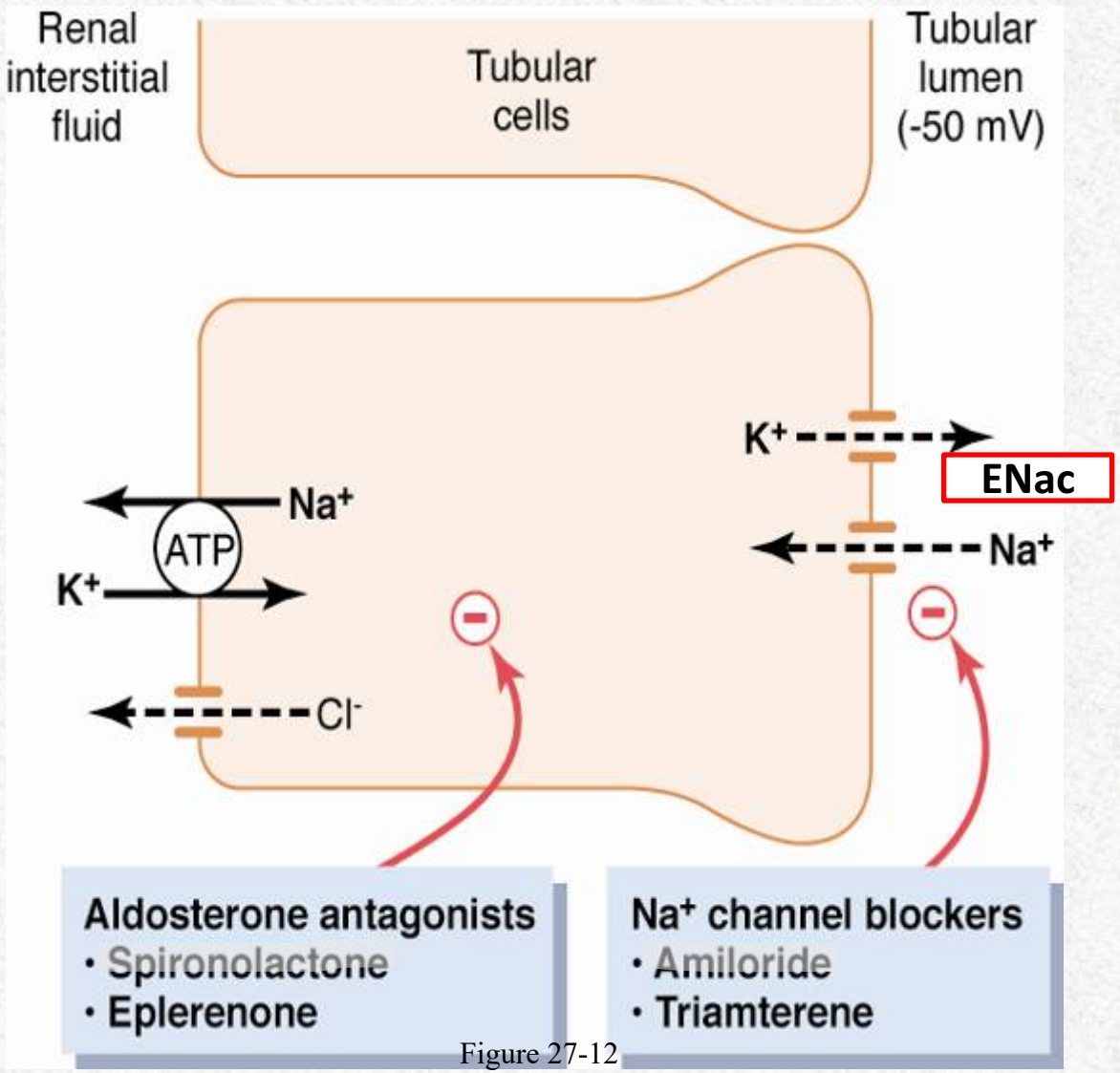
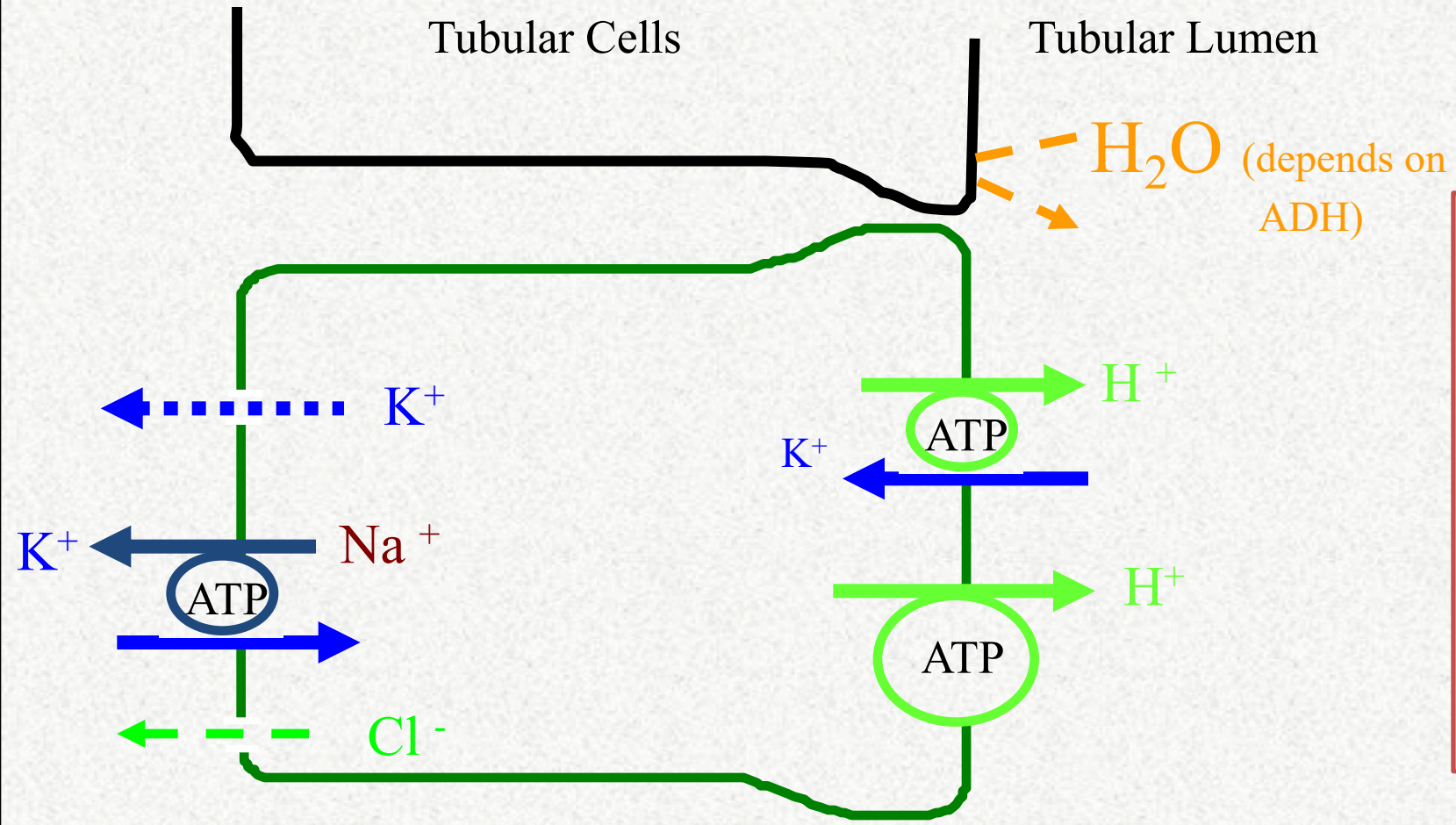


Figure 27-12

There are drugs that act as antagonists for the aldosterone (mineralocorticoid) receptors. When this drug antagonizes this receptor, this causes inhibition of aldosterone and this results in diuresis and increases potassium; it is spared.

ONLY HIGHLIGHTED IS REQUIRED

Late Distal and Cortical Collecting Tubules Intercalated Cells –Secrete H^+



- If we have acidosis in the body then we have high secretion of hydrogen ions through the H+-ATPase.
- When there is alkalosis in the body ten then the transporters change their position in order to correct the alkalosis. In this case, there is secretion of bicarbonate and absorption of H+.

Transport characteristics of medullary collecting ducts

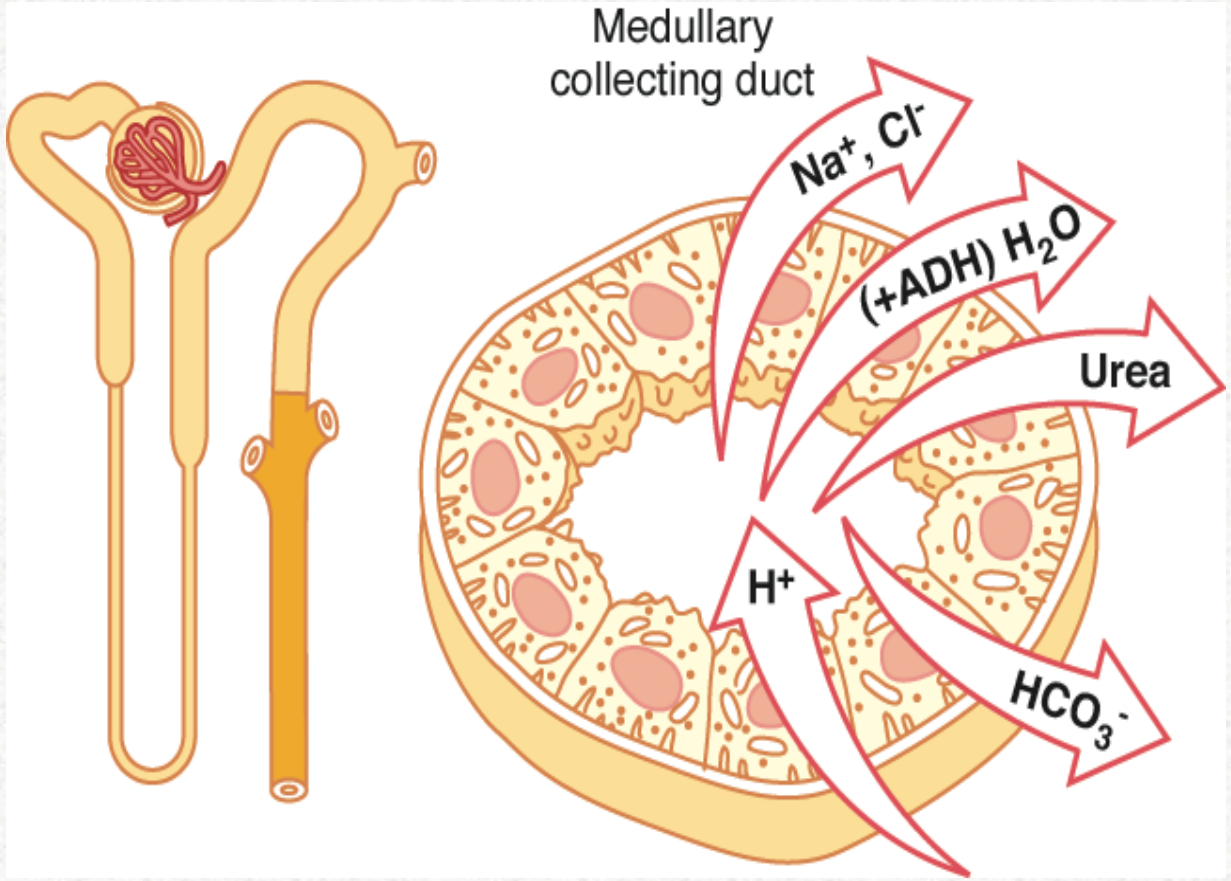
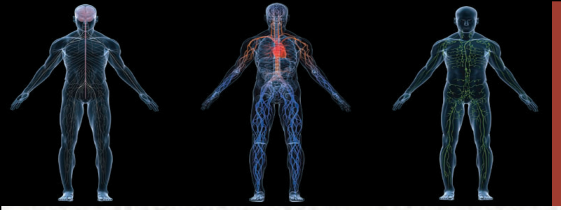
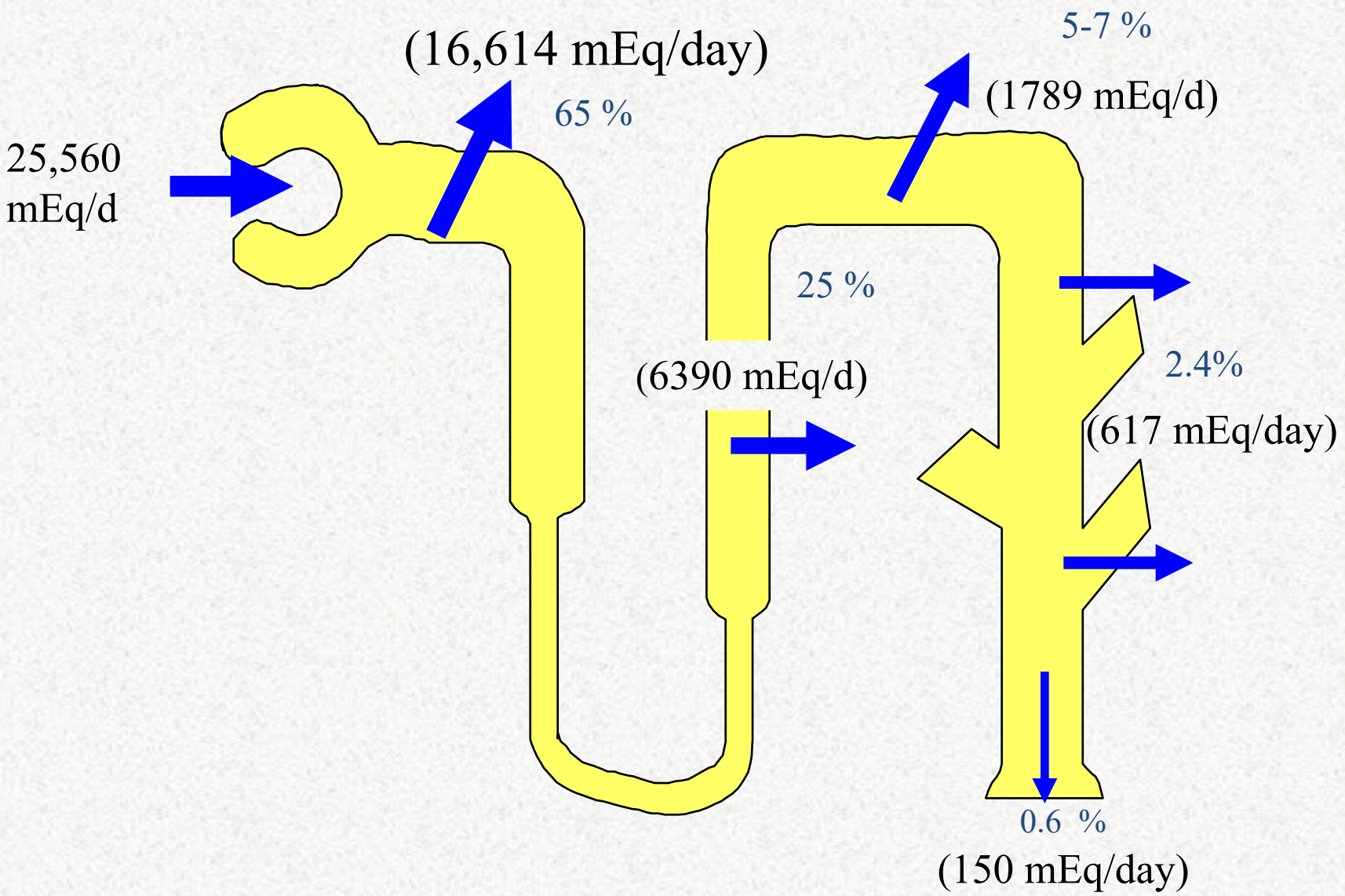


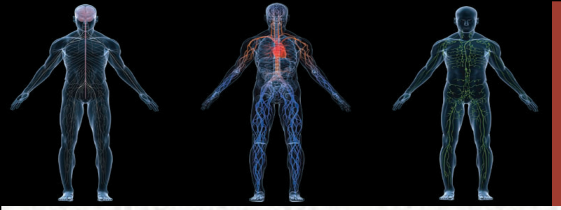
Figure 27-13

- These tubules are in the last stages of urine modification.
- It is characterized by being highly permeable to urea because it has selective transporters for urea and so there is reabsorption of urea because of its high concentration in the tubular fluid.
- Very little of the urea that is reabsorbed goes into the blood, while most of it stays in the interstitial fluid. This causes an increase in the osmolality of the matrix, so when there is ADH, this causes an increase in the efficiency of water reabsorption (higher driving force) because the gradient is higher due to the higher osmolality of the matric (interstitial fluid).
- So, the medullary collecting tubules have an important role in the concentration of the urine when ADH is present, to preserve fluids.



Normal Renal Tubular Na^+ Reabsorption



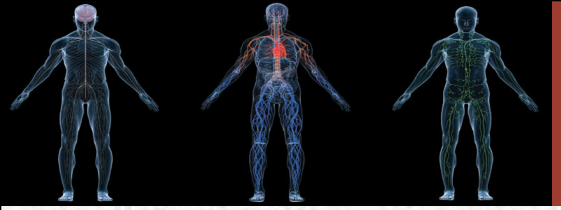


Concentrations of solutes in different parts of the tubule depend on relative reabsorption of the solutes compared to water

- If water is reabsorbed to a greater extent than the solute, the solute will become more concentrated in the tubule (e.g. creatinine, inulin)

Inulin is a material from outside the body that is used to measure the GFR. It is used for this because it is freely filtered not reabsorbed or secreted so that its excretion rate is the same as the filtration.

- If water is reabsorbed to a lesser extent than the solute, the solute will become less concentrated in the tubule (e.g. glucose, amino acids)



Changes in concentrations of substances in the renal tubules

- This graph represents the tracing of substances along the whole nephron
- If the ratio increases, then that means either water is reabsorbed much more than this substance or that it is being secreted from the capillaries into the tubules, so it depends on the segment and if it is permeable to water.

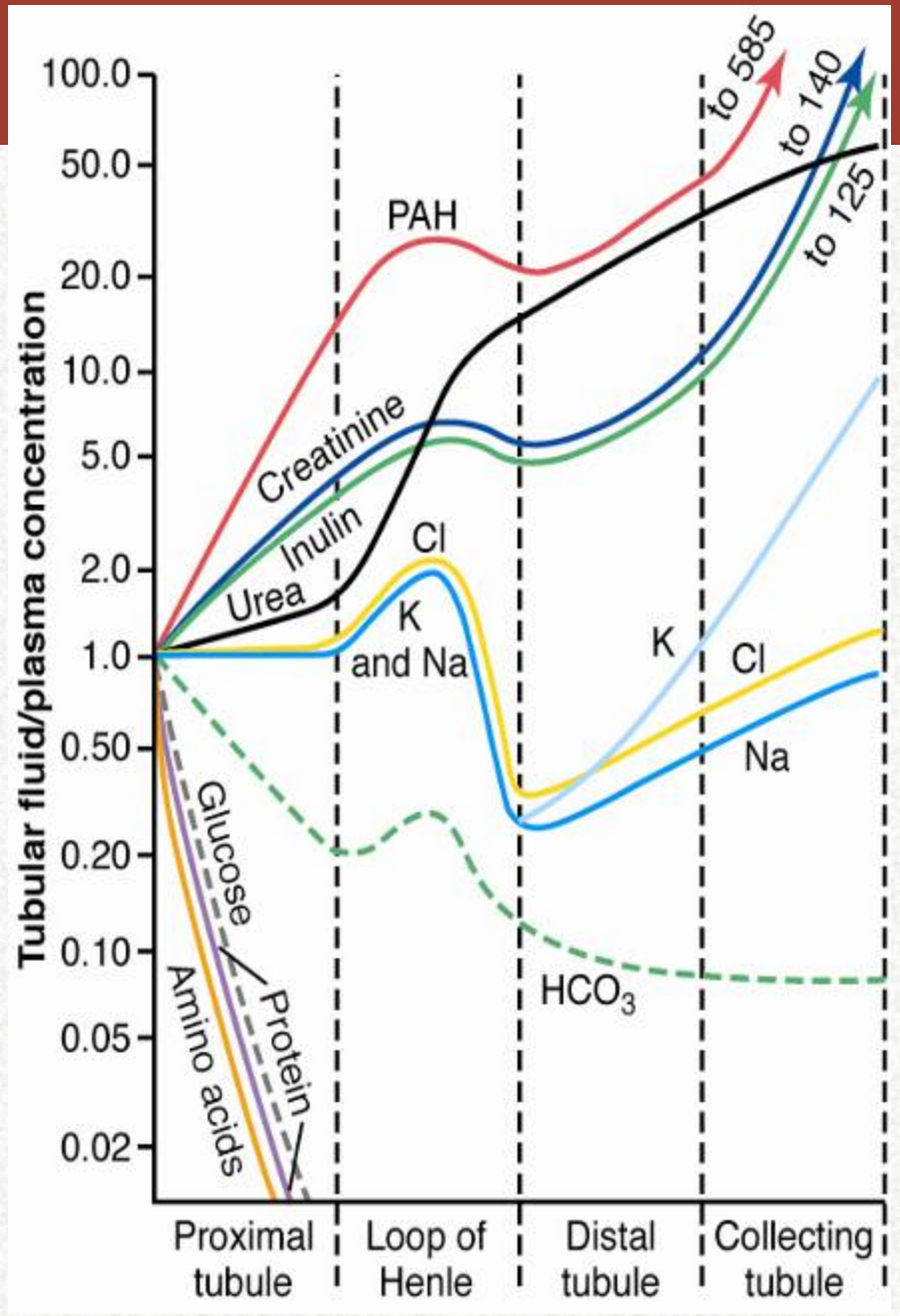
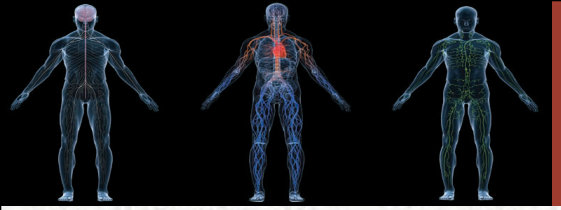


Figure 27-14

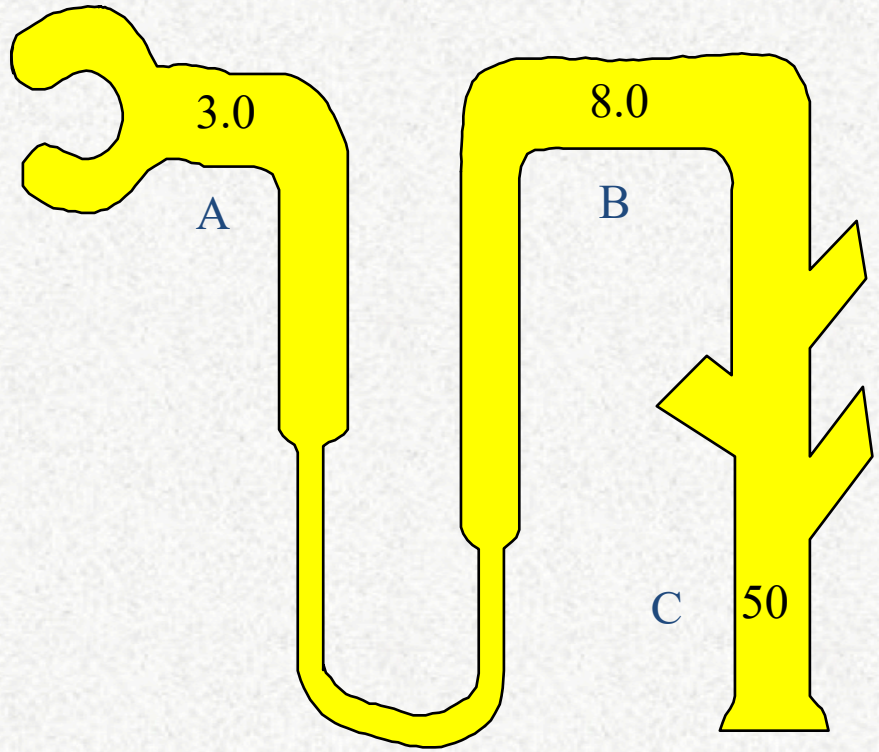


The figure below shows the concentrations of inulin at different points along the tubule, expressed as the tubular fluid/plasma (TF/P_{inulin}) concentration of inulin. If inulin is not reabsorbed by the tubule, what is the percentage of the filtered water that has been reabsorbed or remains at each point ? What percentage of the filtered water has been reabsorbed up to that point?

A = 1/3 (33.33 %) remains
66.67 % reabsorbed

B = 1/8 (12.5 %) remains
87.5 % reabsorbed

C = 1/50 (2.0 %) remains
98.0 % reabsorbed



When we measure the concentration of inulin in different segments, then we will notice that its concentration differs in each segment and that depends on the reabsorption of water in these segments.
The ratio of inulin to water is supposed to be 1, because it is freely filtered with water, so the concentration of inulin represents the ratio of water absorbed. (in A 1/3)